REMARKS

Claims 1-8, 10-16, 19-27 and 30-33 are pending and under examination. Claims 1, 2, 6, 16, 19, 21-23, 30 and 33 have been amended. Support for the amendments can be found throughout the application as filed. Support for the amendments to claims 1, 6, 19, 23, 30 and 33, directed to a flux balance analysis model of cellular metabolism of an organism, can be found, for example, in the preamble of each claims. Support for the amendments to claims 1, 6, 19, 30 and 33, directed to a regulation matrix, can be found at, for example, page 11, paragraph 3 through the paragraph bridging pages 12-13, and in Figure 5. Claims 2 and 21 have been amended to delete the phrase "at least a subset." Support for the amendment to claim 22 can be found at, for example, page 7, last sentence through page 8, line 1. Support for the amendment to claims 16 and 32 can be found at, for example, page 14, lines 14-16. Claim 21 also has been amended to correct an obvious informality with respect to the preamble. Claim 30 also has been amended to correct an obvious informality with respect to the antecedent basis for a referenced flux balance analysis model. Accordingly, the amendments do not raise any issues of new matter and entry thereof is respectfully requested. Applicants have reviewed the Office Action mailed April 19, 2007, and respectfully traverse all rejections for the reasons that follow.

REJECTIONS UNDER 35 U.S.C. § 112, FIRST PARAGRAPH

Claims 2 and 21 stand rejected under 35 U.S.C. § 112, first paragraph, for lacking written description allegedly because the phrase "at least a subset" of logic constraints lacks support in the specification. The Examiner alleges that partitioning reactions into subsets and identifying the smallest set of reactions capable of ensuring adequate connectivity is not a full and complete disclosure of the claimed element.

To meet the written description requirement the language of the specification must describe the claimed invention so that one skilled in the art can recognize what is claimed. *Enzo Biochem, Inc., v. Gen-Probe Inc.*, 296 F.3d 1316, 1328 (Fed. Cir. 2002).

Applicants respectfully submit that this condition has been satisfied. In particular, the partitioning of logic constraints into connectivity restraints is one example of a subset that can protect against violation of a kinetic barrier. Further, Applicants previously cited support where connectivity restraints are further partitioned into subsets is another example of a subset of logic constraints that can protect against violation of a kinetic barrier. Nevertheless, to further prosecution Applicants have amended the claims to remove the objected term. Accordingly, this ground of rejection is moot and its withdrawal is respectfully requested.

Claim 22 stands rejected under 35 U.S.C. § 112, first paragraph, for lacking written description allegedly because the phrase "DNA experimental data constraints" lack support in the application. The Office acknowledges that the phrase "DNA microarray experimental data" constraints is supported in the application, but alleges that the rejected phrase fails to support the current claim term.

Applicants maintain that the claimed element is adequately supported in the application as filed because one skilled in the art will recognize that the DNA experimental data constraints can be equally derived from a variety of sources, including microarray array experiments. In light of this understanding, the claims have been amended to recite "DNA microarray experimental data." Accordingly, this ground of rejection is moot and Applicants respectfully request its withdrawal.

REJECTIONS UNDER 35 U.S.C. § 112, SECOND PARAGRAPH

Claims 1-16, 19-27 and 29-33 stand rejected under 35 U.S.C. § 112, second paragraph, for being indefinite allegedly because the phrase "modeling cellular metabolism of an organism" in the preamble of independent claims 1, 6, 19, 23, 29 and 33 is unclear. The Office alleges that the steps of the claims fail to recite any relationship of an FBA model to an organism and therefore, are unclear with respect to the preamble.

Applicants respectfully submit that the claims are sufficiently clear to satisfy the requirements of the second paragraph of § 112. Nevertheless, to more explicitly recite the relationship between the preamble and the claimed FBA model, independent claims 1, 6, 19, 23, 30 and 33 have been amended to recite that the FBA model is a model of cellular metabolism of the organism. Accordingly, this ground of rejection is now moot and its withdrawal is respectfully requested.

Claims 16 and 32 stand rejected under 35 U.S.C. § 112, second paragraph, for being indefinite allegedly because the phrase "based on" is unclear with respect to the relationship between the recited engineered change and the desired metabolic outcome.

Applicants submit that the claims are clear as written. Nevertheless, claims 16 and 32 have been amended to explicitly recite that the engineered change is made in the organism to produce the desired metabolic outcome. Accordingly, the claims satisfy the precision requirement of the second paragraph of § 112 and withdrawal of this ground of rejection is respectfully requested.

Claim 30 stands rejected under 35 U.S.C. § 112, second paragraph, for being indefinite allegedly because it is unclear whether the flux balance analysis model recited in the last two lines refers to the initial or the altered flux balance analysis model.

Applicants submit that the claim is clear as written. However, claim 30 has been amended to explicitly recite that the referenced flux balance analysis model refers to the altered model. Accordingly, the amendment renders this ground of rejection moot and its withdrawal is respectfully requested.

REJECTIONS UNDER 35 U.S.C. § 102

Claims 1-8, 12-15, 19, 22-23, 25-27, 30, 31 and 33 stand rejected under 35 U.S.C. § 102 for allegedly being anticipated by Palsson et al., US 2002/0012939. The Examiner alleges that Palsson describe logic constraints because paragraphs 054 and 059 purportedly describe constraints defined by a relationship between the amount of a substrate and specific uptake rates, which meets the definition recited in claim 8. The Examiner further alleges that the distinction of applying the constraints in combination with linear equations is moot allegedly because the claims do not recite that linear equations can not be used. The Examiner additionally alleges that the argument with respect to stoichiometric boundaries and a regulation matrix also is moot because the claims do not recite these elements.

Applicants respectfully point out that claim 8 is a dependent claim to claim 6. Therefore, any alleged "definition" purported to be found in this claim should not form the basis of a rejection to independent claims 1, 19, 23, 30 or 33. Further, the recited element of claim 8 further limits the base claim and, although it includes all of claim 6's elements, it does not define the term "logic constraints" as claimed. Rather, the specification defines the meaning of claim terms.

Additionally, Applicants respectfully point out that the claims recite <u>applying</u> logic constraints to a flux balance analysis model to produce <u>an altered</u> flux balance analysis model.

As pointed out in Applicants previous response, the claimed logic constraints are computational logic constraints as illustrated in, for example, Figure 5 and described at, for example, pages 11-13. Such constraints are <u>applied</u> to a flux balance analysis model to produce <u>an altered</u> model. Palsson does not describe applying <u>logic constraints</u> as defined in the application and claimed to produce an <u>altered</u> flux balance analysis model. Moreover, Palsson also does not describe applying constraints as claimed in any of claims 1, 6, 19, 23 or 33 to produce <u>an altered</u> flux balance analysis model that improves predictive capabilities on an initial model.

With respect to the Examiner's view that the claimed logic constraints will not be construed to include a regulation matrix, Applicants respectfully point out that the meaning of a claim term "is its meaning to the ordinary artisan after reading the entire patent." *Phillips v. AWH Corp.*, 415 F.3d 1303, 1321 (Fed. Cir. 2005) (*en banc*). To not construe the term "logic constraints" to include a regulatory matrix is contrary to Federal case law precedent. Nevertheless, the claims now explicitly recite the meaning of logic constraints as defined in the application. Palsson neither teaches the claimed logic constraints nor does Palsson teach applying such logic constraints to produce an altered flux balance analysis model. Accordingly, this ground of rejection is moot and Applicants respectfully request its withdrawal.

CONCLUSION

In light of the Amendments and Remarks herein, Applicants submit that the claims are in condition for allowance and respectfully request a notice to this effect. Should the Examiner have any questions, she is invited to call the undersigned attorney.
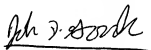
This is a request under the provision of 37 CFR § 1.136(a) to extend the period for filing a response in the above-identified application for three months from July 19, 2007 to October 19,

2007. Applicant is a small entity; therefore, please charge Deposit Account number 26-0084 in the amount of $525.00 to cover the cost of the three-month extension. Any deficiency or overpayment should be charged or credited to Deposit Account 26-0084.

This amendment accompanies the filing of a Request for Continued Examination (RCE). Please charge Deposit Account No. 26-0084 the amount of $405.00 for the RCE per the attached transmittal. No other fees or extensions of time are believed to be due in connection with this amendment; however, consider this a request for any extension inadvertently omitted, and charge any additional fees to Deposit Account No. 26-0084.

Reconsideration and allowance is respectfully requested.

Respectfully submitted,

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